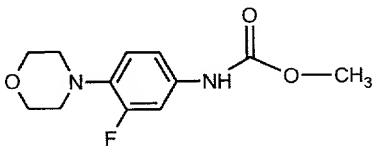
## EXAMPLES

The following detailed examples describe how to prepare the various compounds and/or perform the various processes of the invention, and are to be construed as merely illustrative, and not limitations of the preceding disclosure in any way whatsoever. Those skilled in the art will recognize appropriate variations from the procedures both as to reactants and as to reaction conditions and techniques.

## EXAMPLE 1




**Preparation of N-Carbomethoxy-3-fluoro-4-morpholinylaniline (Compound I, $R^1$ = 3-Fluoro-4-morpholinylphenyl)**

**Step A: 3-Fluoro-4-morpholinylaniline**

3,4-Difluoronitrobenzene (25.196 g, 158.38 mmol) was added to a mixture of morpholine (60.0 ml, 688 mmol, 4.34 eq) in THF (30 ml) at -14°C. The mixture was permitted to warm to 10°C, then maintained at 10-13°C for 1 hr. A mixture of citric acid monohydrate (75 g, 357 mmol, 2.25 eq) in water (365 ml) was added with a concomitant exotherm to 28°C. The phases were separated, and the aqueous phase was washed with toluene (95 ml). The organic phase was washed with water (315 ml), then concentrated under reduced pressure. Toluene (46 ml) and methanol (60 ml) were added, followed by palladium on carbon (5%, 50% water wet, 3.1603 g, 0.7426 mmol, 0.00469 eq), and the mixture was sealed in a Parr shaker. Hydrogen pressure (40 psi) was applied and maintained while agitating for 42 min. The catalyst then was removed by filtration under reduced pressure, and washed with

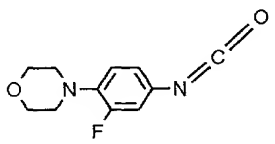
toluene (60 ml). Heptane (150 ml) added to the filtrate and the resultant slurry concentrated under reduced pressure. Heptane (300 ml) was added, and the precipitate collected by filtration under reduced pressure, washed with heptane, and dried to give the title compound, HPLC (stationary phase is 4.6 x 250 mm Zorbax RX C-8 column; mobile phase is acetonitrile (650 ml), triethylamine (1.85 ml) and acetic acid (1.30 ml) and water of sufficient amount to make 1,000 ml; flow rate = 3.0 ml/min; UV detection at 254 nm) RT = 1.08 min, > 99.3 area); $^1$H- NMR (Pyridine-$d_5$) δ: 2.95-2.98, 3.80-3.83, 5.38, 6.68, 6.78 and 6.90 ; CMR (Pyridine-$d_5$) 52.43, 67.33, 103.31, 110.63, 121.29, 130.80, 146.23 and 157.72 .

**Step B: N-Carbomethoxy-3-fluoro-4-morpholinylaniline (Compound I, $R^1$ = 3-Fluoro-4-morpholinylphenyl)**

3,4-Difluoronitrobenzene (24.967 g, 156.94 mmol) was added to a mixture of morpholine (60.0 ml, 688 mmol, 4.38 eq) in THF (30 ml) at -6°C. The mixture was permitted to warm to 10° over 2 hrs, then maintained at 10°C for 1/2 hr. A mixture of citric acid monohydrate (75 g, 357 mmol, 2.27 eq) in water (365 ml) was added with concomitant exotherm to 28°. The phases were separated, and the aqueous washed with toluene (95 ml). The organic phases were washed with water (315 ml), the aqueous back wash extracted with toluene (95 ml), and concentrated under reduced pressure. Toluene (76 ml) and methanol (60 ml) were added, followed by palladium on carbon (5%, 50% water wet, 3.1370 g, 0.7371 mmol, 0.00470 eq), and the mixture sealed in a Parr shaker. Hydrogen pressure (40 PSI) was applied and maintained while agitating for 4.5 hrs. The catalyst then was removed by filtration under reduced pressure, and washed with toluene (100 ml). The mixture was cooled to 2°C, and a mixture of aqueous potassium carbonate (47%, 17.1 ml, 85 mmol, 0.54 eq) and water (150 ml) was added. Methyl chloroformate (16.4 ml, 212 mmol, 1.35 eq) then was added while maintaining the temperature at about 3-3.5°. The resultant slurry was permitted to warm to 20-25°C, then stirred 17 hrs. The mixture is warmed to 75° to give a solution, then cooled to 46°, heptane (333 ml) added, then the mixture cooled to 0°C, the precipitate collected by filtration with reduced pressure, washed with heptane (100 ml cooled to 5°C) then water (230 ml cooled to 5°C), and dried to

give Compound I, wherein $R^1$ = 3-fluoro-4-morpholinylphenyl, TLC (silica gel; methanol/methylene chloride, 5/95) Rf = 0.74 (one spot); $^1$H- NMR ($CDCl_3$) δ: 3.03, 3.76, 3.86, 6.75, 6.87, 6.98, 7.27; CMR (CDCl3) 51.18, 52.42, 67.03, 107.81, 114.56, 119.00, 133.25, 135.77, 154.07, 155.70.

## EXAMPLE 2



**Preparation of 3-Fluoro-4-morpholinylphenylisocyanate (Compound VI, $R^1$ = 3-Fluoro-4-morpholinylphenyl)**

A mixture of 3-fluoro-4-morpholinylaniline (Example 1, 12.01 g, 61.21 mmol) in methylene chloride (100 ml) was added to a mixture of phosgene (1.93 M in toluene, 63.4 ml, 122.4 mmol, 2.00 eq) in p-chlorotoluene (60 ml) over 15 min, while maintaining a temperature of about -12 to 3°C. The material was rinsed in with methylene chloride (30 ml). The mixture then was warmed to 130°C under atmospheric pressure with concomitant distillation of methylene chloride, phosgene, toluene, and hydrogen chloride gas into a caustic scrubber. The mixture was cooled to 25°C and filtered. The precipitate was washed with methylene chloride (3 x 15 ml). The filtrate was concentrated under reduced pressure. Heptane (200 ml) was added to the concentrated filtrate, and the resultant slurry cooled to -32°C. The product was collected by filtration with reduced pressure, washed with heptane, cooled to -30°C, and dried in a nitrogen stream to give Compound VI, wherein $R^1$ = 3-fluoro-4-morpholinylphenyl, HPLC (stationary phase is 4.6 x 250 mm Zorbax RX C-8 column; mobile phase is acetonitrile (650 ml), triethylamine (1.85 ml) and acetic acid (1.30 ml) and water of sufficient amount to make 1,000 ml; flow rate = 3.0 ml/min; UV detection at 254 nm) RT = 1.08 min. Upon derivatizing as N-carbomethoxy-3-fluoro-4-morpholinylaniline by dissolving in methanol; $^1$H- NMR ($CDCl_3$) δ: 3.05, 3.86 and 6.78-6.89 ; CMR ($CDCl_3$) 50.90, 66.89, 113.11, 119.15,